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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/611,914	07/03/2003	Eyal Talor	CS-120	5597

7590 02/27/2004

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EXAMINER
NICKOL, GARY B

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 02/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/611,914	TALOR, EYAL	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-41* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Petition

The petition to make this application (10/611914) special under 37 C.F.R. 1.102 filed July 30, 2003 has been granted.

Claims 1-41 are pending.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

1. Claims 1-12, drawn to a method for pre-sensitizing cancer prior to therapeutic treatment comprising administering a therapeutically active amount of specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ and GM-CSF to IL-2, classified in class 424, subclass 198.1.

2. Claims 13-23, drawn to a method for inducing tumor cells into a cell cycle selected from the group of G_1, S, G_2 and M comprising administering a therapeutically active amount of specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ and GM-CSF to IL-2, classified in class 424, subclass 198.1.

3. Claims 24-27, drawn to a serum-free and mitogen-free cytokine mixture comprising specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ and GM-CSF to IL-2 and pharmaceutical composition thereof, classified in class 530, subclass 351; class 514, subclass 2.

4. Claims 26-28, drawn to a pharmaceutical composition for use in treating cancer comprising specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ GM-CSF, and **IL-3** to IL-2, classified in class 514, subclass 2; class 530, subclass 351.

5. Claims 26-27, 29, as specifically drawn to a pharmaceutical composition for use in treating cancer comprising specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ GM-CSF, and **IL-6** to IL-2, classified in class 514, subclass 2; class 530, subclass 351.

6. Claims 26-27, 30, as specifically drawn to a pharmaceutical composition for use in treating cancer comprising specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ GM-CSF, and **IL-8** to IL-2, classified in class 514, subclass 2; class 530, subclass 351.

7. Claims 26-27, 31, as specifically drawn to a pharmaceutical composition for use in treating cancer comprising specific ratios of cytokines selected from the group

of IL-1β, TNF-α, IFN-γ GM-CSF, and **IL-1α** to IL-2, classified in class 514, subclass 2; class 530, subclass 351.

8. Claims 26-27, 32, as specifically drawn to a pharmaceutical composition for use in treating cancer comprising specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ GM-CSF, and **IL-10** to IL-2, classified in class 514, subclass 2; class 530, subclass 351.

9. Claims 26-27, 33, as specifically drawn to a pharmaceutical composition for use in treating cancer comprising specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ GM-CSF, and **IL-16** to IL-2, classified in class 514, subclass 2; class 530, subclass 351.

10. Claims 26-27, 34, as specifically drawn to a pharmaceutical composition for use in treating cancer comprising specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ GM-CSF, and **G-CSF** to IL-2, classified in class 514, subclass 2; class 530, subclass 351.

11. Claims 26-27, 35, as specifically drawn to a pharmaceutical composition for use in treating cancer comprising specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ GM-CSF, and **TNF-β** to IL-2, classified in class 514, subclass 2; class 530, subclass 351.

12. Claims 26-27, 36, as specifically drawn to a pharmaceutical composition for use in treating cancer comprising specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ GM-CSF, and **MIP-1α** to IL-2, classified in class 514, subclass 2; class 530, subclass 351.

13. Claims 26-27, 37, as specifically drawn to a pharmaceutical composition for use in treating cancer comprising specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ GM-CSF, and **MIP-1β** to IL-2, classified in class 514, subclass 2; class 530, subclass 351.

14. Claims 26-27, 38, as specifically drawn to a pharmaceutical composition for use in treating cancer comprising specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ GM-CSF, and **RANTES** to IL-2, classified in class 514, subclass 2; class 530, subclass 351.

15. Claims 26-27, 39, as specifically drawn to a pharmaceutical composition for use in treating cancer comprising specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ GM-CSF, and **EGF** to IL-2, classified in class 514, subclass 2; class 530, subclass 351.

16. Claims 26-27, 40, as specifically drawn to a pharmaceutical composition for use in treating cancer comprising specific ratios of cytokines selected from the group

of IL-1β, TNF-α, IFN-γ GM-CSF, and **PGE_2** to IL-2, classified in class 514, subclass 2; class 530, subclass 351.

17. Claims 26-27, 41, as specifically drawn to a pharmaceutical composition for use in treating cancer comprising specific ratios of cytokines selected from the group of IL-1β, TNF-α, IFN-γ GM-CSF, and **TxB_2** to IL-2, classified in class 514, subclass 2; class 530, subclass 351.

The inventions are distinct, each from the other because of the following reasons:

Groups 1 and 2, although similar in that they comprise administering the same composition, represent independent and or distinct methods because they differ in their objectives, method steps, and criteria for success. For example, Group I is specific to sensitizing cancer cells *prior* to a therapeutic modality, including, but not limited to, chemotherapy, immunotherapy, and radiation therapy. Group II, however, is drawn to a method of inducing tumor cells to enter a particular cycle of the cell cycle such as G_1, S, G_2, and M. Furthermore, an examination of the two Groups would require different searches in the literature and different considerations when considering patentability issues under 35 USC 112, 1st paragraph.

The inventions of Groups 3-17 represent separate and distinct products which are chemically distinct and which may have different modes of operation, different functions and different effects. Although Groups 3-17 contain a common mixture of specific ratios of cytokines, they also each contain a distinct molecule (i.e. IL-3, IL-6, IL-1α) which imparts independence to the

multitude of pharmaceutical compositions. Not only is there a burden in searching each and every ratio of the different cytokine mixtures in the literature, but there is the added burden of examining each composition, individually, as it applies to an effective pharmaceutical composition, under the rules governing 35 USC 112, 1st paragraph. Not all cytokines are functionally equivalent, and it would require undue searching and examination to consider all of the different pharmaceutical compositions in one examination.

The invention of Group 3 and the methods of Groups 1 and 2 are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (I) the process for using the product as claimed can be practiced with another materially different product or (ii) the product as claimed can be used in a materially different process of using that product [see *MPEP* § **806.05(h)**]. In the instant case, the mixture of cytokines as claimed can be used in materially different processes such a method for pre-sensitizing cancer prior to therapeutic treatment and or a method for inducing tumor cells into a cell cycle selected from the group of G_1, S, G_2 and M.

The invention of Groups 4-17 and the methods of Groups 1-2 are not at all related because the distinct cytokine pharmaceutical compositions of Groups 4-17 are not used in the methods of Groups 1 and 2.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as

indicated is proper. Moreover, because these inventions are distinct for the reasons given above and the search required for one group is not required for another group, restriction for examination purposes as indicated is proper.

Note:

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the

application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.
Examiner
Art Unit 1642

GBN

GARY NICKOL
PRIMARY EXAMINER